Amendments to the Specification

Amend paragraph [01] at page 1 as follows:

This application claims priority from U.S. Provisional Application No. 60/429,743 filed November 26, 2002 and the U.S. Provisional Application ~~with attorney docket number 05882.0156.PZUS03~~60/508,149 filed September 30, 2003, each of which is hereby incorporated by reference in its entirety.

Amend paragraph [34] at page 8 as follows:

Figure 2 depicts an alignment of the amino acid sequences from Figure 1 (SEQ ID NOS: 1-12) that highlights sequence substitutions in the five humanized antibodies relative to the murine original (IIA1).

Amend paragraph [35] at page 8 as follows:

Figure 3 depicts: (A) IIA1 V_H nucleic acid sequence (SEQ ID NO: 13) and amino acid sequence (SEQ ID NO: [[1]]46); (B) IIA1 V_L nucleic acid sequence (SEQ ID NO: 14) and amino acid sequence (SEQ ID NO: [[7]]47).

Amend paragraph [71] at page 14 as follows:

The terms "identical" or percent "identity," in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (i.e., about 60% identity, preferably 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity over a specified region, when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection (see, e.g., NCBI web site ~~http://~~www.ncbi.nlm.nih.gov/BLAST/ or the like). Such sequences are then said to be "substantially identical." This definition also refers to, or may be applied to, the complement of a test sequence. The definition also includes sequences that have deletions and/or additions, as well as those that have substitutions, as well as naturally occurring, e.g., polymorphic or allelic variants, and man-made variants. As described below, the preferred algorithms can account for gaps and the like. Preferably, identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length.

Amend paragraph [74] at page 15 as follows:

Preferred examples of algorithms that are suitable for determining percent sequence identity and sequence similarity include the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al., Nuc. Acids Res.* 25:3389-3402 (1977) and Altschul *et al., J. Mol. Biol.* 215:403-410 (1990). BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available

through the National Center for Biotechnology Information (~~http://~~www.ncbi.nlm.nih.gov~~/~~). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul et al., supra). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, e.g., for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff & Henikoff, Proc. Natl. Acad. Sci. USA 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

Amend paragraph [160] at page 44 as follows:

Recombinant antibody variable domains occasionally contain undesired alternative mRNA splice sites, which can then give rise to alternately spliced mRNA species. Such sites could, in theory, exist in the murine variable domain but only become active in the context of a heterogeneous expression cell and/or new acceptor sites from chimeric constant regions. Taking advantage of codon degeneracy to remove potential alternative splice sites while leaving the encoded amino acid sequence unchanged may eliminate such undesired alternative splicing. To detect any potential alternative splice sites in the M200 V_H and V_L mini-exons, the initial designs were analyzed with a splice site prediction program from the Center for Biological Sequence Analysis from the Technical University of Denmark (~~http://~~www.cbs.dtu.dk/services/NetGene2/). For both 200-M mini-exons, the correct donor splice sites were identified; however, potential alternative donor splice sites were detected in CDR3 of the V_H mini-exon and CDR1 of the V_L mini-exon. To eliminate the possibility of these splice sites being used, single silent base pair changes were made to the mini-exon designs. In the case of the V_H design, a silent GGT to GGA codon change at glycine 100 (Kabat numbering) was made; for the V_L design, a silent GTA to GTC codon change at valine 29 was made. In both cases these silent changes eliminated the potential secondary splicing donor signal in the V-genes.

After the ABSTRACT section at page 61, please insert the paper copy of the SEQUENCE LISTING submitted herewith.